



文献综述

补肾活血中药治疗多囊卵巢综合征导致排卵障碍性不孕患者的临床研究进展

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摘要: 多囊卵巢综合征是育龄女性常见内分泌疾病, 发病机制复杂, 以高雄激素血症、排卵障碍和卵巢多囊样改变为主要特征, 严重影响患者生殖健康与生活质量, 是排卵障碍不孕症主因。中医认为多囊卵巢综合征的病机核心为肾虚与血瘀, 治疗应以补肾活血为主。补肾活血中药具有多靶点调节作用。补肾活血中药在治疗多囊卵巢综合征相关排卵障碍性不孕中的理论基础、临床应用及现代药理机制。研究发现, 该中药可通过调控下丘脑-垂体-卵巢轴、可改善卵巢功能、调节性激素水平、改善胰岛素代谢、促进卵泡发育与排卵, 并调节多条信号通路, 如 PI3K/AKT/mTOR、MAPK、TGF- β 1/SMAD 等, 从而在提高受孕率、改善妊娠结局方面展现出显著疗效。此外, 补肾活血中药在联合西药治疗中也表现出协同增效作用, 能显著改善子宫内膜容受性, 降低流产率。因此, 本文系统梳理并总结了有关补肾活血中药用于治疗多囊卵巢综合征患者排卵障碍性不孕患者的临床研究进展, 旨在为其规范化、科学化的临床应用提供更为坚实且可信的循证依据。

关键词: 多囊卵巢综合征; 补肾活血; 排卵障碍; 不孕; 中药

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前言

多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 作为一种常见的妇科内分泌疾病。^[1] 该病在育龄女性中具有较高的发病率, 其确切病因尚未明确, 但普遍认为遗传因素与环境因素在其发生发展中起着关键作用。^[2] 临床主要表现为高雄激素血症 (hyperandrogenemia, HA) 所致的多毛、痤疮、肥胖, 以及排卵障碍引起的月经稀发、闭经等症状,^[3] 以及卵巢多囊样改变等特征, 严重影响患者的生殖健康与生活质量, 已成为排卵障碍不孕的最主要原因。^[4] 目前关于 PCOS 的发病机制主要, 为下丘脑-垂体-卵巢轴功能紊乱, 会导致促性腺激素 (gonadotropin, Gn) 和促黄体生成素分 (luteinizing hormone, LH) 分泌紊乱,

引发卵巢过度分泌雄激素。^[5] 为改善排卵障碍、促进妊娠, 迫切需要探索更优治疗路径。在中医药治疗 PCOS 具有多靶点、调节全身平衡的特点, 其核心病机在中医理论中多归因于肾虚与血瘀。近年来, 补肾活血中药能改善卵巢功能、调节内分泌失衡方面展现出良好疗效, 为 PCOS 相关不孕的治疗提供了新的思路。本文通过综述形式探讨补肾活血中药治疗 PCOS 导致排卵障碍性不孕中的临床应用与现代药理机制, 以期临床实践提供理论依据与参考。

1. 中医对 PCOS 的认识

PCOS 在中医学中的“月经后期”、“闭经”、“崩漏”、“不孕症”范畴。中医理论认为, 肾为

先天之本，主藏精，司生殖，其盛衰直接影响女性“肾-天癸-冲任-胞宫”生殖轴的功能状态。肾气充盈，则天癸适至、任脉通畅、太冲脉盛，月事如期，具备孕育能力。若肾精亏虚，肾气不足，则该生殖轴失衡，冲任气血乏源，胞宫失养，易致月经失调、排卵障碍，进而影响生育功能。一方面，正如《医宗金鉴·妇科心法要诀》指出：“肾虚冲任亏，胞宫失养，月事后期，甚至闭经”。说明肾虚可直接导致冲任气血化生乏源，胞宫失于濡养，表现为月经后期、闭经等，此为该病发生之基础。^[6-8] 另一方面，正如《医林改错》指出：“元气既虚，必不能达于血管，血管无气，必停留而瘀”。肾中元气亏虚，无力推动血行，必然造成血行迟缓、脉络瘀阻，从而形成血瘀。而瘀血一旦形成，又会反过来阻滞冲任经脉，阻碍肾精的输布与肾气的化生，形成恶性循环，进一步加剧肾虚。因此，肾虚为 PCOS 发病之本，血瘀则是在肾虚基础上形成的关键病理环节，二者互为因果、相互影响，共同导致生殖轴的功能紊乱。此种紊乱临床上主要表现为月经失调与排卵障碍，正如《备急千金要方》中表明的：“妇人者，众阴所集，常与湿居，十四以上，阴气浮溢，百想经心，内伤五脏，外损姿颜，月水去留，前后交互，瘀血停凝，中道断绝，其中伤堕不可具论矣。然五脏虚实交错，恶血内漏，气脉损竭……”，若气血运行不畅，便易可见该病所致不孕的病机核心，^[9] 在于肾虚血瘀交织所致的病理失衡。

2. 补肾活血类中药的理论基础

PCOS 的中医病机核心在于“肾虚为本，血瘀为标”。肾主藏精、司生殖，肾精亏虚则天癸不至、冲任失调，导致月经紊乱与排卵障碍；血瘀则阻滞胞脉，进一步影响卵泡发育与排出，因此，补肾活血中药为治疗 PCOS 排卵障碍性不孕的为主。^[10,11] 在临床实践中，补肾活血中药疗效显著，已得到多项研究证实。^[12-14] 根据 Yuan BC, 等^[15] 研究统计结果，临床常用的补肾类中药常用以菟丝子与枸杞子协同配伍，温补肾阳，滋养肾阴，调和阴阳、充养精血，以助生殖功能恢复；桑寄生与川续断则善于

补肝肾、强筋骨，稳固胎元，为调经助孕。活血类中药常用以泽兰、牛膝、鸡血藤均能活血祛瘀，通经活络。^[16] 名老中医的经验也为该治法提供了重要支持。例如朱南孙教授强调 PCOS 以“肾虚痰瘀”为核心，创立“朱氏调经方”，以熟地黄、菟丝子、覆盆子等补肝肾，填精益髓，佐以当归、丹参活血调经，动静结合，共奏调经种子之效。^[17,18] 马堃教授则在补肾之余，全程辅以川芎、赤芍、制香附等等活血化瘀药，能够疏调气机，促进血液流畅，祛瘀生新，改善妇科盆腔内环境，有助于卵泡的发育与排出。^[19]

补肾中药具有类似内分泌激素的作用，能双向调节女性性腺轴，恢复卵巢功能与排卵节律。^[20] 现代药理学研究进一步从科学角度阐释了补肾活血中药的多靶点作用机制。补肾类药物如菟丝子总黄酮可提升雌激素水平，促进卵泡发育；枸杞多糖能改善胰岛素抵抗 (insulin resistance, IR)，调节性激素紊乱；^[15,21] 淫羊藿苷则通过调控下丘脑-垂体-卵巢轴及 PI3K/AKT、MAPK 等信号通路，改善卵巢功能与卵泡质量。^[22,23] 活血类中药通过调节细胞增殖与凋亡而发挥治疗作用，Li SD, 等^[24] 的研究已证实了这一机制。具体而言，由川牛膝等组成的中药复方对伴有不孕或不良妊娠史的 PCOS 患者具有显著疗效；泽兰可改善血液循环，清除卵巢局部炎症因子，从而优化卵泡微环境，减轻卵巢组织病变，并促进排卵。^[25,26] 此外，丹参、川芎等活血药能增强卵巢局部血流、抗炎抗氧化、改善卵泡膜结构及卵母细胞质量；泽兰、牛膝等则可调节细胞增殖与凋亡，促进卵泡正常发育与排出。在复方配伍中，补肾药与活血药相辅相成，形成“补肾促发育、活血助排出”的协同效应。例如，“菟丝子+丹参”组合兼具补肾与活血之功，既能促进卵泡生长，又可改善卵巢血供与排卵功能；“枸杞子+川芎”则以滋肾配行气活血，有助于调节内分泌水平并改善子宫内膜容受性，从而提升受孕率与妊娠结局。综上所述，补肾活血中药治疗 PCOS 不孕，既遵循中医“肾虚血瘀”的病机理论，又通过

现代研究揭示了其多成分、多通路、整体调节的作用机制。

3. 补肾活血类中药的作用机制

3.1 对生殖内分泌的调节作用

3.1.1 调节激素水平

PCOS 可能是由于促性腺激素 (Gn) 的分泌失调, 以及促性腺激素释放激素 (gonadotropin-releasing hormone, GnRH) 分泌模式的异常变化所致。这种情况导致黄体化激素 (LH) 相对于卵泡刺激素 (follicle-stimulating hormone, FSH) 的比例过高。^[27] LH 刺激卵巢分泌雄激素 (androgen), 而 FSH 不足则会影响颗粒细胞中的芳香化酶 (aromatase) 的活性, 从而阻碍雄激素转化为雌二醇 (estradiol, E2), 持续性的异常转化作用会对下丘脑和垂体产生长期的负反馈效应, PCOS 女性表现出异常的负反馈机制。^[27] 雄激素在卵泡早期生长中扮演着关键角色。然而, 当雄激素过量时, 会抑制与卵丘扩张和卵母细胞成熟相关的基因表达, 最终导致小卵泡过多的生成。^[28] 这些种失衡可能进一步影响卵巢的正常发育以及女性的生育功能。多项研究表明, 能补肾活血药对 Gn 水平也有调节作用, 促进卵泡的正常发育与排卵。Yao YJ^[29] 运用补肾活血药治疗 PCOS 导致排卵障碍性不孕的患者, 研究结果显示, 观察组在治疗后, 观察组总有效率 97.1% 高于对照组 82.9%; LH、FSH、黄体生成素和卵泡刺激素的比例 (LH/FSH)、睾酮 (testosterone, T)、E2 等均出现明显改善效果, 说明补肾活血中药能有效调整血清性激素, 副作用小。Zhao YX, Wang CY^[30] 使用补肾活血方治疗的 PCOS 不孕患者, 研究发现观察组 LH、T 水平均较对照组更低, 证明补肾活血方对于 PCOS 患者体内性激素水平具有明显调控作用, 可有效改善机体激素紊乱, 调节月经并促使排卵正常, 以提高妊娠率。Ma YP^[31] 采用补肾活血中药治疗 PCOS 导致排卵障碍性不孕患者, 研究结果显示观察组总有效率 92.1% 高于对照组 84.2%, 表明补肾活血中药能提高妊娠发生率, 改善患者激素指标, 具有较高的治疗成效。

3.1.2 改善胰岛素抵抗

胰岛素抵抗 (insulin resistant, IR) 可通过作用于垂体、卵巢和肝脏诱发高雄激素血症 (hyperandrogenemia, HA), 体外研究表明, 胰岛素可刺激卵巢细胞 (theca cell)。卵泡细胞是卵巢中的细胞, 主要功能是产生雄激素, 而在 PCOS 的女性中, 卵泡膜细胞功能异常, 导致雄激素分泌过多。^[32] 同样, 胰岛素可通过促肾上腺皮质激素 (adrenocorticotrophic hormone, ACTH) 的刺激, 增强肾上腺雄激素的分泌, 并降低血清性激素结合蛋白 (sex hormone-binding globulin, SHBG) 水平, 从而提高游离雄激素的浓度。因此, IR 可通过多种途径促进 PCOS 患者的 HA 发生。^[33] 补肾活血类中药可通过多种途径改善 IR。Chen Y, 等^[33] 运用益肾活血化痰汤辅助治疗 PCOS 不孕伴 IR 疗效确切, 能纠正糖代谢紊乱及性激素紊乱, 减轻 IR 及 HA, 改善临床症状, 提高自然受孕率。Tao C, 等^[34] 使用补肾活血方对 PCOS-IR 型大鼠性激素水平及 IR, 研究结果能改善 PCOS-IR 大鼠性激素水平和 IR。

由此可见, 补肾活血类中药通过调节激素水平和改善 IR, 对 PCOS 患者的排卵障碍性不孕具有显著疗效。研究表明, 这类中药可调节生殖内分泌, 降低雄激素, 改善 IR 等方面, 显著提高排卵率与妊娠率, 为 PCOS 患者提供了安全有效的治疗方案。

3.2 对卵巢微环境与促进卵泡发育排卵

PCOS 的排卵障碍根源于卵巢功能的紊乱。其核心病理包括卵巢局部高雄激素血症、胰岛素抵抗及异常的卵泡微环境, 这些因素共同导致卵泡发育阻滞、大量小卵泡积聚及排卵失败。^[32] 补肾活血中药通过多靶点作用, 一方面改善卵巢的整体功能状态 (微环境), 另一方面直接促进卵泡的最终成熟与排出。在改善卵巢微环境方面, 该中药旨在纠正卵巢内部的病理基础。研究表明, 补肾活血方能有效提升肾虚血瘀型 PCOS 患者的卵巢功能, 改善基础 FSH 水平, 优化卵泡募集的启动条件。^[35] 动物实验进一步揭示, 其作用机制可能与调节卵泡膜细胞和颗粒细胞

功能有关,能有效降低卵巢局部雄激素水平,改变卵泡膜细胞层厚度,从而为卵泡的健康发展清除障碍。^[36]在直接促进卵泡发育与排卵方面,该中药则侧重于解决“最终环节”的问题。中医认为肾虚推动无力兼夹血瘀阻滞,是卵子难以排出的关键。名老中医夏桂成教授创制的补肾促排卵汤即以“补肾为本,促排为标”,通过温补肾阳、养阴益精、调畅气血而促进排卵。^[5]Wang RY^[37]的临床研究显示,补肾活血方可减少卵巢囊性卵泡数量、提高排卵率与妊娠率。其促排卵机制在动物模型中得到阐明:该中药可恢复PCOS大鼠的动情周期,促进卵泡最终成熟,增加排卵率,并减少卵泡闭锁。^[38]

现代药理学为此提供了科学解释:方中活血化瘀药能显著增加卵巢组织局部血流量,这一方面有助于改善卵巢包膜的厚度与张力,为卵子排出扫除物理障碍;另一方面也促进了补肾药效成分的输送与吸收,从而协同发挥“促排卵、健黄体”的关键作用。^[5]综上所述,补肾活血中药并非单一环节的作用,而是通过综合改善卵巢微环境与直接推动排卵进程的双重机制,标本兼治,有效恢复PCOS患者的正常排卵功能,最终实现妊娠目标。

3.3 对妊娠结局的影响

在PCOS的患者中,虽然妊娠率已有显著改善,但妊娠结局仍然低于非PCOS患者。抗苗勒氏管激素(anti-müllerian hormone, AMH)被认为是预测PCOS患者妊娠结局的重要指标,研究显示PCOS女性血清AMH水平通常较高。^[39]临床上应用补肾活血中药,通过调节内分泌功能、改善排卵障碍,可进一步提高受孕率。Kuang GC,等^[40]运用补肾活血汤合桂枝茯苓片对PCOS的AMH及对妊娠率影响,结果显示该方案能使临床妊娠率显著提高。Chen QX,等^[41]研究发现,补肾活血汤联合克罗米芬可改善肥胖型PCOS不孕症患者的IR及相关炎症因子水平,使妊娠率由37.25%提高至45.10%,表明能有效提高受孕率。补肾活血汤能改善卵巢功能,促进受精卵着床,从而提高妊娠成功率。^[42,43]

此外,PCOS患者即使成功妊娠,仍面临较高的流产风险,常伴随IR、孕激素抵抗(progesterone resistance, PR)和HA等内分泌异常。Yang XF,等^[44]发现在着床窗期PCOS患者的E2和孕激素(progesterone, P)分泌不足,导致子宫内膜形态异常,分泌反应减弱,进而降低子宫内膜容受性,这可能是其流产率较高的主要原因。补肾活血中药通过改善子宫内膜容受性、调节母胎免疫平衡等机制,有助于降低流产风险。Wang RY,等^[45]使用补肾活血方治疗肾虚血瘀型PCOS不孕患者,结果显示该方能改善子宫内膜血流灌注与形态,降低T水平,提升子宫内膜容受性及临床妊娠率。类似地,Chen SS, Zhang N^[46]的研究也表明,在PCOS患者冻融胚胎移植(frozen embryo-transfer, FET)周期中,补肾活血方可降低子宫动脉血流阻力,改善子宫内膜容受性,从而提高妊娠率并优化妊娠结局。

3.4 调节信号通路

3.4.1 PI3K/AKT/mTOR 信号通路

磷脂酰肌醇3-激酶/蛋白激酶B/哺乳动物雷帕霉素靶蛋白(phosphoinositide 3-kinase/protein kinase B/mammalian target of rapamycin signaling, PI3K/AKT/mTOR)信号通路在调节卵巢功能、卵泡发育及代谢紊乱中发挥重要作用,而该信号通路的异常激活是PCOS的重要致病机制之一。PI3K/AKT信号通路是PI3K/AKT通路是诱发IR的关键机制,其信号障碍可致葡萄糖摄取异常。^[47]AKT/mTOR信号通路异常会导致女性卵巢病变,影响卵泡发育,甚至导致不孕。^[48,49]胰岛β细胞功能缺陷与IR和PCOS患者卵巢及子宫内膜该信号通路受损密切相关。^[50,51](见图1)

补肾活血中药可通过激活PI3K/AKT/mTOR信号通路,调节PCOS患者的激素水平,能改善IR,促进卵泡发育和排卵,从而有效治疗PCOS。^[52,53]Tao C,等^[34]发现补肾活血方通过激活卵巢AKT/mTOR信号通路,改善PCOS-IR大鼠的胰岛素抵抗和性激素紊乱,表现为FSH、E2升高,LH、T、AMH降低,从而促进卵泡发育

与排卵，缓解内分泌失调所致不孕。Jiang XF，等^[54]发现补肾助孕汤，其中有补肾活血药，可通过促进 PI3K-/AKT/mTOR 信号通路的磷酸

化来抑制卵巢颗粒细胞凋亡，从而保护卵泡发育，改善卵巢功能。

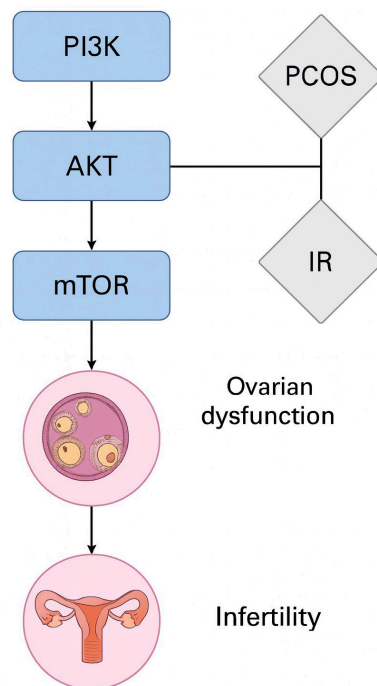


图 1 PI3K/AKT/mTOR 信号通路在 PCOS 中的作用机制图

3.4.2 MAPK 信号通路

丝裂原活化蛋白激酶 (mitogen-activated protein kinase, MAPK) 信号通路是细胞信号传递的关键环节，通过从细胞表面传输信号到细胞核，调节 Gn 的转录。^[55] MAPK 信号通路与子宫内

膜相关生殖疾病有关，在 PCOS 患者中活性更高。^[56] 目前 MAPK 信号通路：包括 ERK、JNK、p38 MAPK 三个主要分支异常已被证实与 PCOS 发病相关，靶向这些通路为治疗 PCOS 提供了一种潜在途径。^[57] (见图 2)

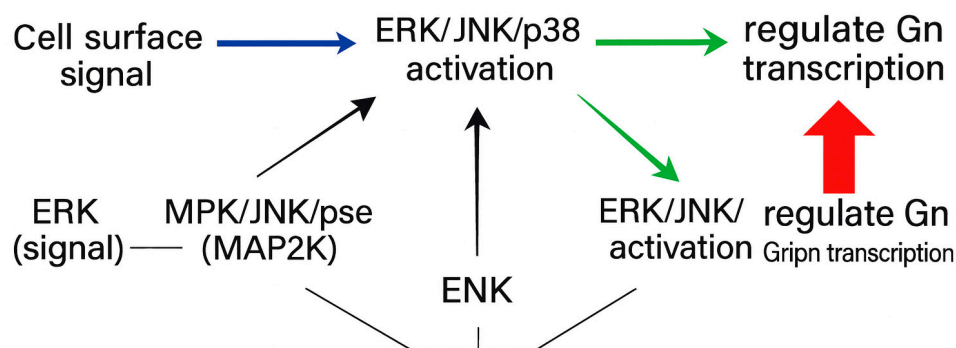


图 2 MAPK 信号通路在 PCOS 中的作用机制图

补肾活血中药为 PCOS 治疗，其活性成分可作用 MAPK 信号通路，调节该通路关键蛋白表达，纠正激素失衡，改善患者排卵及代谢障碍。菟丝子总黄酮通过抑制 MAPK/ERK 信号通路的异常激活来发挥其改善 PCOS 激素失调和排卵障碍等的生理作用。^[58] 丹参-郁金可根据预测所得主要活性成分通过 MAPK 信号通路进行实验验证，为中药治疗 PCOS 提供依据。^[59] Shi XK, 等^[60] 研究发现，木犀草素和木犀草素-7-甲基醚通过直接作用于细胞内的 TPL2，从而下调磷酸化的 p38 MAPK 通路蛋白，抑制 MKK3/6-p38 MAPK-CREB 轴实现的。木犀草素和木犀草素-7-甲基醚还可以减少囊性卵泡，恢复性激素水平，从而有效改善小鼠 PCOS 症状。^[57] 而在动物实验中也观察到益肾调经丸，方中有多种药物活性成分能够调节性激素水平，还可通过调节 MAPK/ERK 信号通路作用于 PCOS 模型大鼠。^[61] 这些研究表明，多种活性成分可通过调控 MAPK 信号通路改善 PCOS 的激素失调与排卵障碍，从而缓解因排卵功能障碍导致的不孕，最终促进性激素水平恢复并改善排卵功能。

3.4.3 TGF- β 1/SMAD 信号通路

转化生长因子- β 1/SMAD (transforming growth factor- β 1/SMAD Signaling, TGF- β 1/SMAD) 信号通路是 TGF- β 1 促进卵巢多囊化，并与间质纤维化加重 PCOS 相关，TGF- β 1 受体的下游信号转导因子 SMAD 在卵巢多囊化过程中发挥重要的作用，是 PCOS 卵巢功能障碍的关键调控机制之一。^[62] Yan X, 等^[62] 研究发现，六味地黄丸可能通过调节 TGF- β 1/SMAD 信号通路，抑制 TGF- β 1、SMAD2 和 SMAD3 的 mRNA 表达，从而降低大鼠血清 T、FSH 和 LH 水平，改善内分泌代谢功能，并消除卵巢内多囊样扩张及异常卵泡，最终有效缓解和改善 PCOS 的症状。Wang XD, 等^[63] 研究表明，补肾促排卵汤通过调控 TGF- β 1/SMAD 信号通路缓解 PCOS 相关卵巢纤维化，同时改善卵泡发育，降低血清 T、LH 水平，促进卵巢功能修复。Zhang WQ, 等^[64] 研究表明，补肾调经方可通过调节 TGF- β 1/SMAD 信号通路，改善 PCOS 大鼠的性激素水平，促进卵泡发育与排卵，改善卵巢形态，能助于缓解因排卵障碍导致不孕。(见图 3)

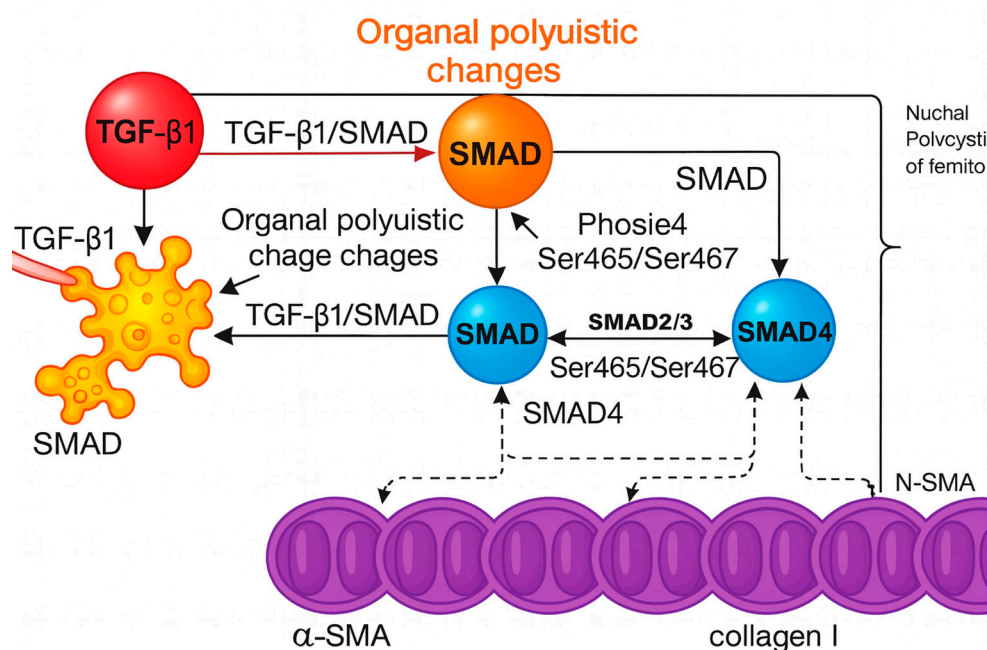


图 3 TGF- β 1/SMAD 信号通路在 PCOS 中的作用机制图

3.4.4 TLR4/NF- κ B 信号通路

Toll 样受体 4/核因子 κ B (toll-like receptor 4, TLR4/ nuclear factor kappa-light-chain-enhancer of activated B cells, NF- κ B) 信号通路对 PCOS 机制的影响。该信号通路是一种与体内炎症反应密切相关的信号通路。在 PCOS 患者中,该通路的过度激活可能导致卵巢慢性炎症,从而引发激素紊乱、卵泡发育障碍而不孕。因此,抑制该信号通路,有望成为治疗 PCOS 及恢复卵巢功能的有效途径。Liu F, 等^[65]

研究表明抑制 TLR4/NF- κ B 信号可减轻 PCOS 小鼠炎症 IR 和生殖异常。补肾活血中药通过调控该信号通路发挥改善 PCOS 的关键作用。红景天苷 (salidroside, Sal) 是从植物红景天中提取的活性成分,具有抗炎、抗氧化及免疫刺激活性等药理作用。^[66] 研究显示 Sal 可能通过抑制 HMGB1/TLR4/NF- κ B 信号通路改善 PCOS 大鼠性激素平衡和卵巢组织损伤,保护卵巢功能,促进卵泡发育,从而为恢复排卵与提升生育力创造有利条件。^[67] (见图 4)

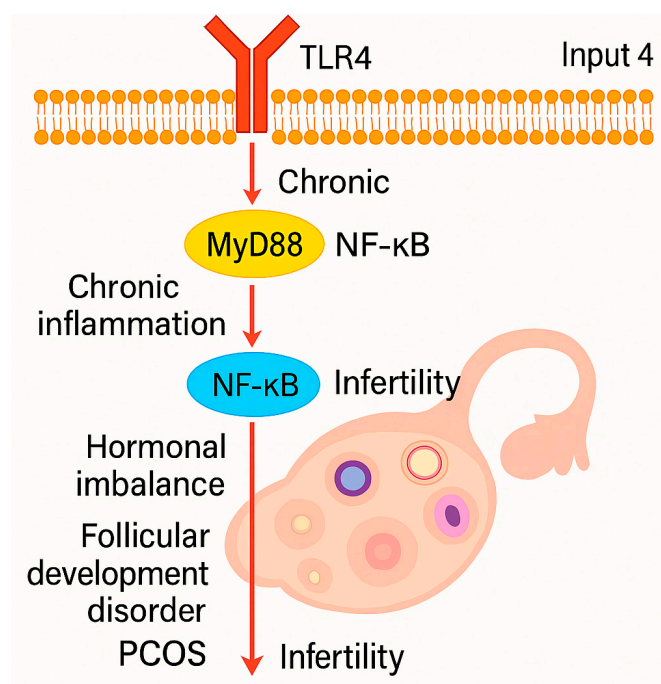


图 4 TLR4/NF- κ B 信号通路在 PCOS 中的作用机制图

3.4.5 其他信号通路

3.4.5.1 AMPK 信号通路

腺苷酸活化蛋白激酶 (AMP-activated protein kinase, AMPK) 信号通路作为细胞代谢的核心调节因子,对于细胞功能的维持至关重要。研究表明 PCOS 大鼠的不孕可能源于 AMPK 信号通路受阻,从而导致线粒体损伤。^[67] 补肾活血中药可能通过激活 AMPK 来改善 PCOS 相关的代谢异常。Tian JY, 等^[68] 研究发现,归肾丸加味可调控 AMPK/Akt/Nrf2 信号通路有助于改善 PCOS 大鼠的糖脂代谢紊乱与氧化应激,优化卵巢微环境,促进卵泡发育与功能恢复,从而实现规律排卵,提升生育能力。另外,芍药苷是芍药

科植物提取的活性成分。研究表明,芍药苷对 PCOS 大鼠可能通过调控 AMPK/SIRT1/PGC-1 α 信号通路促进 PCOS 卵巢颗粒细胞增殖,并抑制细胞凋亡,同时,能促进血清 E2 和 P 水平升高,表明芍药苷对改善 PCOS 大鼠的激素分泌具有积极作用。^[69]

3.4.5.2 AGE-RAGE 信号通路

晚期糖基化终产物 (advanced glycation end products, AGE) 与晚期糖基化终产物受体 (receptor for advanced glycation end products, RAGE) 信号通路,是调控氧化应激和炎症的重要通路。^[70] AGE 积累会影响血清激素的生成,损害卵母细胞的成熟,降低卵细胞的

质量, 可能导致 PCOS。而患有 PCOS 的女性与正常女性相比, 体内卵泡膜和颗粒细胞层中 AGE 和 RAGE 表达增加。^[71] He JL, 等^[72] 研究显示, 滋肾育胎丸可升高 E2、P 水平, 降低 LH、T 水平, 抑制 VEGF 过度表达, 同时减少子宫组织中 RAGE 的表达, 以促进肾虚证型 PCOS 大鼠优势卵泡的成熟与排卵。Huang JG, 等^[73] 研究发现, 坤泰胶囊 (Kuntai capsules, KTC) 是一种中药制剂, 在促进 PCOS 患者排卵、调节激素水平、改善卵巢功能等方面具有积极作用, 其作用机制之一是通过调控 AGE-RAGE 信号通路, 从而恢复卵巢排卵与内分泌功能, 最终有助于治疗 PCOS 相关的不孕。

3.4.5.3 SDF-1/CXCR4 信号通路

基质细胞衍生因子-1 (stromal cell-derived factor 1, SDF-1) 作为趋化因子受体 4 (C-X-C chemokine receptor type 4, CXCR4) 的特异性配体, 与其结合后激活 SDF-1/CXCR4 信号通路, 参与细胞增殖与凋亡的调节, 同时趋化炎症细胞, 触发炎症反应。^[74] 补肾活血药在调节该信号通路方面可能对 PCOS 产生积极影响。淫羊藿苷是淫羊藿的主要活性成分, 具有显著的抗炎作用, 并能提升卵巢功能。^[75,76] 此外, 淫羊藿苷可降低 PCOS 模型大鼠卵巢细胞的凋亡率, 同时促进卵巢储备功能减退患者卵巢颗粒细胞增殖。^[77,78] Xu QF, 等^[79] 研究发现, 淫羊藿苷可能通过抑制 SDF-1/CXCR4 信号通路, 对 PCOS 大鼠有助于促进卵巢颗粒细胞增殖、抑制其凋亡, 该通路从而改善卵泡发育微环境, 提升卵泡质量与成熟度, 进而为恢复正常的排卵功能基础, 助于治疗 PCOS 相关的不孕。因此, 提示淫羊藿苷可能是一种具有治疗 PCOS 潜力的有效药物。

结论

PCOS 是导致排卵障碍性不孕的主要病因, 其核心病机“肾虚血瘀”为中医治疗提供了明确的理论方向。本综述归纳了补肾活血中药通过多靶点、整体调节的作用特点, 在 PCOS 不孕治疗中展现出特色疗效。大量临床研究表明,

该类中药不仅能通过调节性激素水平、改善胰岛素抵抗、促进卵泡发育与排卵, 还能通过调控多条信号通路, 直接促进卵泡发育, 并改善子宫内膜容受性, 最终实现提高排卵率与改善妊娠率、降低流产率的临床目标。尤其在与西药 (如来曲唑) 一线促排卵药物联合使用时, 可显著提高受孕率并优化妊娠结局, 展现出中西医结合的独特优势。综上所述, 补肾活血中药在 PCOS 排卵障碍性不孕治疗中具有明确的理论价值和临床潜力。

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บทความปริทัศน์

ความก้าวหน้าด้านการวิจัยทางคลินิกเกี่ยวกับการใช้ยาสมุนไพรจีนประเภทบำรุงไตและกระตุ้นการไหลเวียนเลือดในการรักษาภาวะมีบุตรยาก เนื่องจากความผิดปกติของการตกไข่ในผู้ป่วยกลุ่มอาการถุงน้ำรังไข่หลายใบ

สิรภัทร รัตนกระจำง, หวัง อี้อิง, สวี จื่อเว่ย, หนิง จิ้ง, หลี่ อี้เจิง, เฉิน เคอ, จาง ชิน, ซี นั่ว, เฉิน จิ้ง
โรงพยาบาลการแพทย์แผนจีนแห่งนครเซี่ยงไฮ้ สังกัดมหาวิทยาลัยการแพทย์แผนจีนเซี่ยงไฮ้

บทคัดย่อ: กลุ่มอาการถุงน้ำรังไข่หลายใบเป็นโรคทางระบบต่อมไร้ท่อที่พบได้บ่อยในผู้หญิงในวัยเจริญพันธุ์ มีสาเหตุและกลไกการเกิดที่ซับซ้อน มีลักษณะสำคัญ คือ ภาวะฮอร์โมนเพศชายในเลือดสูง ความผิดปกติของการตกไข่ และมีการเปลี่ยนแปลงผิดปกติของรังไข่ทำให้งไข่มีถุงน้ำหลายใบ ส่งผลกระทบอย่างมากต่อสุขภาพการเจริญพันธุ์ คุณภาพชีวิตของผู้ป่วย และเป็นสาเหตุหลักของภาวะมีบุตรยากจากความผิดปกติของการตกไข่ ตามแนวคิดของการแพทย์แผนจีน กลไกการเกิดโรคของกลุ่มอาการถุงน้ำรังไข่หลายใบมีพยาธิสภาพหลักอยู่ที่ไตพร่องร่วมกับเลือดคั่ง ดังนั้นหลักการรักษาควรเน้นที่การบำรุงไตและกระตุ้นการไหลเวียนเลือด ยาสมุนไพรจีนที่มีสรรพคุณบำรุงไตและกระตุ้นการไหลเวียนเลือดมีฤทธิ์ในการปรับสมดุลหลายเป้าหมาย งานวิจัยได้อธิบายถึงพื้นฐานทางทฤษฎีการประยุกต์ใช้ทางคลินิก และกลไกทางเภสัชวิทยาสมัยใหม่ของยาสมุนไพรกลุ่มนี้ในการรักษาภาวะมีบุตรยากจากความผิดปกติของการตกไข่ที่สัมพันธ์กับกลุ่มอาการถุงน้ำรังไข่หลายใบ โดยพบว่ายาสมุนไพรสามารถออกฤทธิ์ผ่านการปรับสมดุลแกนไฮโปทาลามัส-ต่อมใต้สมอง-รังไข่ ช่วยฟื้นฟูการทำงานของรังไข่ ปรับระดับฮอร์โมน แก้ไขความผิดปกติของการเผาผลาญอินซูลิน กระตุ้นการเจริญของไข่และการตกไข่ รวมถึงมีบทบาทในหลายเส้นทางสัญญาณ เช่น PI3K/AKT/mTOR, MAPK, TGF- β 1/SMAD เป็นต้น ส่งผลให้มีประสิทธิภาพเด่นชัดในการเพิ่มอัตราการตั้งครรภ์และปรับปรุงผลลัพธ์การตั้งครรภ์ นอกจากนี้ การใช้ร่วมกับยาสมัยใหม่ยังแสดงฤทธิ์เสริมฤทธิ์ร่วมกัน โดยสามารถเพิ่มความสามารถในการฝังตัวของตัวอ่อนและลดอัตราการแท้งได้อย่างมีนัยสำคัญ บทความฉบับนี้ รวบรวมผลงานวิจัยมุ่งเน้นการศึกษาทางคลินิกเกี่ยวกับการใช้ยาสมุนไพรจีนที่มีฤทธิ์บำรุงไตและกระตุ้นการไหลเวียนเลือดในการรักษาภาวะมีบุตรยากเนื่องจากความผิดปกติของการตกไข่ในผู้ป่วยกลุ่มอาการถุงน้ำรังไข่หลายใบ เพื่อเสริมสร้างหลักฐานเชิงประจักษ์ที่มีความน่าเชื่อถือสำหรับการประยุกต์ใช้ในทางคลินิกต่อไป

คำสำคัญ: กลุ่มอาการถุงน้ำรังไข่หลายใบ; บำรุงไตและกระตุ้นการไหลเวียนเลือด; ความผิดปกติของการตกไข่; ภาวะมีบุตรยาก; ยาสมุนไพรจีน

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Review Article

Clinical research progress on the efficacy of kidney tonifying and blood activating Chinese herbal medicine in treating ovulation disorder related infertility in patients with polycystic ovary syndrome

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Abstract: Polycystic ovary syndrome (PCOS) is a common endocrine disorder among women of reproductive age. Its pathogenesis is complex, with the main characteristics being hyperandrogenism, ovulatory dysfunction, and polycystic ovarian changes. It severely affects patients' reproductive health and quality of life and is a leading cause of anovulatory infertility. Traditional Chinese medicine (TCM) considers the core pathogenesis of PCOS to be rooted in kidney deficiency and blood stasis, with treatment primarily focused on tonifying the kidney and promoting blood circulation. Chinese herbal medicines with these properties exhibit multi-target regulatory effects. Their theoretical foundation, clinical applications, and modern pharmacological mechanisms in treating anovulatory infertility associated with PCOS have been extensively explored. Studies have shown that such herbal therapies can regulate the hypothalamic-pituitary-ovarian axis, improve ovarian function, balance sex hormone levels, enhance insulin metabolism, promote follicular development and ovulation, and modulate multiple signaling pathways, including PI3K/AKT/mTOR, MAPK, and TGF- β 1/SMAD. These mechanisms contribute significantly to improved conception rates and pregnancy outcomes. Moreover, when combined with Western medicine, these herbs demonstrate synergistic effects, notably enhancing endometrial receptivity and reducing miscarriage rates. This article compiles research focusing on clinical studies of kidney tonifying and blood activating traditional Chinese herbal medicine in the treatment of ovulation disorder related infertility in patients with polycystic ovary syndrome, with the aim of providing more robust and reliable evidence to support future clinical applications.

Keywords: polycystic ovary syndrome; kidney tonifying and blood activating; ovulation disorders; infertility; Chinese herbal medicines

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